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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,078	01/21/2004	Klass P. Hardeman	047446/273072	4620

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/762,078	HARDEMAN ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/18 & 8/6/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/18 & 8/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

No claims have been cancelled, no claims have been amended, the disclosure has not been amended, and no new claims have been added as of the mailing date of this Office action. Two Information Disclosure Statements (2 IDSs) filed June 18, 2004 and August 6, 2004 have been received with all cited references and made of record.

Claims **1-31** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-31** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for a limited number of nucleotides linked though a termal phosphate group to a solid support and the synthesis thereof, does not reasonably provide enablement for the vast array of compounds, some linked to a solid support and some not linked to a solid support, and the synthesis thereof, encompassed by instant claims **1-30**, and to the method of testing encompassed by claim **31**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The reliance of the independent claims on incompletely defined or non-defined terminology renders the claim vastly over broad in scope.

B. The nature of the invention: The invention is directed to compounds wherein a terminal 5'-nucleotidyl unit with optionally multiple O-P-O linkages is attached to an intermediate linker or linkers and these linkers are ultimately alternatively attached to a solid support, "a tag," or "a protective group." The invention is also directed to methods of making these compounds, and to a method of testing apparently based on affinity chromatography wherein the above noted compounds, when attached to a solid support, play a key role in the

analysis of proteomes; aka mixtures of compounds derived from the internal components of intact cells following disruption.

C. The state of the prior art: Affinity chromatography is well known in the prior art, but presently there is no single reference which discloses all of the details of the instant claimed compounds, their method of making, or their application in affinity chromatography.

D. The level of one or ordinary skill: One of ordinary skill would not find the syntheses or the affinity chromatography methods disclosed herein to be difficult to execute if the compounds being used therefore are as well defined as provided for in the numerous examples found in the disclosure, but would find such exercises much more difficult because of the lack of well defined definitions of the "compound[s]" as presently of record in the claims.

E. The level of predictability in the art: Compounds which structures similar to the prior art affinity chromatography supports are likely to provide results similar to those already established in the prior art. However, this conclusion does not necessarily apply to all of the compounds encompassed by the instant claims.

F. The amount of direction provided by the inventor: The instant disclosure provides a large number of examples of how to make compounds usable in affinity chromatography, but only one prospective description, and no specific embodiments, describing how these compounds might be applied to actual affinity chromatographies.

G. The existence of working examples: As noted above there are many synthetic working examples, but no working examples of how any one of the instant disclosed compounds may be used to carry out affinity chromatography. And also there are no working examples wherein the nucleotidyl moiety is attached to a protecting group or to a "tag."

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be undue because the scope of the compound claims is excessive and because of the total absence of working examples to provide guidance concerning whether the instant compounds actually behave in a predictable manner based on the prior art experience of others with similar affinity chromatographic-capable compounds.

Claims **29 and 30** are objected to because of the following informalities:

Both claim **19** and claim **20** lack proper terminal punctuation.

Both claim **29** and claim **30** lack proper terminal punctuation and also lack the term -- and -- between the last two Markush group members.

Appropriate correction is required.

Claims **1-6, 8, 16-28 and 31** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 1, the term "composition" is technically erroneous because said term implies the presence of two or more separate substances; e.g. the term of art "pharmaceutical composition" requires at least one active ingredient and at least one carrier. Examiner suggests that the term -- compound -- should be substituted for the noted term. See also claims **2-8 and 16-27** wherein the same error is repeated.

In claim **1** at line 1, the term "comprising" is incorrect in the instant claim because said term implies that the chemical structure of the compound being claimed contains additional structural component(s) not defined in the claim. Applicant is respectfully requested to substitute narrow language such as -- consisting of-- or the like for the noted term. Examiner suggests substitution of narrower language (-- consisting of --) for "comprising" at each occurrence because compound claims directed to monomeric substances or monomeric substituents attached to solid supports are inherently narrow in scope. See also claims **2, 3, 4 and 23-27** wherein a similar error occurs.

In claim **1** at lines 3-4, the term "X= 0 or 1" requires that the definitions of R_1 and R_2 be amended to read -- when X = 1 R_1 is a covalent bond between Y and R_2, or when X = 0 R_1 is an acyl group, ... --. Otherwise the definitions includes radicals when for example X = 0 and R_1 is a covalent bond. Alternatively, if applicant intends the claim definitions to include other possibilities, different amendments may be appropriate. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at lines 4-10, the term "substituted" renders the instant claim incompletely defined because the substituents implied thereby have not been defined in the claim. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at lines 8-11, the definitions of variable R_2 is incorrect because it fails to define the substituent moieties as divalent. All of the listed substituent group names are normally considered to be monovalent; e.g. "alkyl," but may be amended to read -- divalent alkyl --, etc. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at line 11, the term "K is a heteroatom" renders the instant claim incomplete because the identity of the moiety has not been specified, and because the necessarily -- divalent -- character of the "atom" has also not been specified. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at line 12, the term "phosphate group mimic" renders the instant claim incompletely defined because the noted term is not further defined in the claim. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at line 13, the term "nucleoside or nucleoside derivative" is technically incorrect because the substituent groups being defined are not compounds but are substituent groups. Examiner suggests that the term be amended to read -- a 5'-nucleosidyl group or a 5'-nucleosidyl group wherein the nucleoside is not naturally occurring -- or the like. Alternatively, the term "derivative" is also not further defined but would be acceptable if a definition of what is meant thereby were inserted into the claim. See also claims **28 and 31** wherein similar errors occur.

In claim **1** at lines 8 and 11, the term "or a combination thereof" renders the claim indefinite because what is meant thereby is not further defined. See also claims **2, 3, 28 and 31** wherein similar errors occur.

In claim **2** at line 1, the term "comprises" is incorrect for the reasons noted above for claim **1** and is incomplete because claim **2** has added subject matter to the definition of variable "R_2" which has not been found in claim **1**. Examiner suggests that the noted term should be amended to read -- further comprising -- in order to give proper notice of the presence of additional subject matter, OR that the entire scope of compound subject matter should be

incorporated into claim **1** so that dependent claims do not need to be relying on a -- further comprising -- claim drafting strategy. See also claim **3** wherein a similar error occurs.

In claim **2** at line 2, the term "a general formula" implies that there are other alternatives not disclosed in the claim. Did applicant intend the term to read -- the general formula --?

In claims **5 and 6** at line 2, the term "nitrogen atom" renders the claim incompletely defined because the group at the third valence of "N" has not been specified.

Claim **8** is improperly dependent because said claim fails to further limit the subject matter of the claim from which it depends.

In claim **21** at line 5, the term "and" is incorrect because the claim appears to have been drafted with the intent that "ionized variant or a salt thereof" would be alternatives not additives. Examiner suggests substitution of the term -- or --.

In claim **22** the term "adenosine, ... and uridine" are directed to compounds, not substituents. Appropriate amendment is respectfully requested. See also claims **23-27** wherein a similar error reoccurs. In addition, the term "analog" in claim **22** is indefinite because there is no further definition of what chemical structures are intended to be included within the scope of the claim. Deletion is suggested.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1-31** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Trayer et al.** (PTO-892 ref. **R**) in view of **Van Aerschot et al.** (PTO-892 ref. **T**).

The instant claims are directed to compounds including a terminal nucleotidyl moiety attached to a solid support by linker(s), to a tag, or to a protecting group, and methods of making same. In addition, the invention is directed to the application of the claimed compounds as adsorbents (aka "mediums") in affinity chromatography.

Trayer et al. discloses the synthesis of numerous adenosine phosphate-type affinity chromatography media and teaches at page 622, column 1 (General Discussion) in addition that the methods disclosed may be used to make analogues of the compounds disclosed.

Trayer et al. does not expressly disclose the particular linker arrangements claimed herein.

Van Aerschot et al. discloses silica adsorbents modified by the attachment of single linkers or combinations of linkers bonded to one another in series for the purpose of attaching a nucleoside or nucleotide unit at the terminus. This reference does not disclose the particular types of solid support derivatized compounds claimed herein.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made, based on the expansive teachings of **Trayer et al.** to make compounds including the linkers of **Van Aerschot et al.** which compounds would read on the instant claimed compounds. And one of ordinary skill, again based on the teachings of **Trayer et al.** would expect that the resultant compounds would be useful in affinity chromatography.

One having ordinary skill in the art would have been motivated to combine these references because the expansive teachings and examples of **Trayer et al.** motivates the combination with other references to generate alternative structures to those of **Trayer et al.** with similar utility in affinity chromatography.

Therefore, the instant claimed compounds, methods of making and method of using would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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09/21/2006

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